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NEWS 7	JUL 09	PATDPAFULL adds Simultaneous Left and Right Truncation (SLART) to AB, CLM, MCLM, and TI fields
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NEWS 9	JUL 27	CA/CAplus enhanced with new citing references
NEWS 10	JUL 16	GBFULL adds patent backfile data to 1855
NEWS 11	JUL 21	USGENE adds bibliographic and sequence information
NEWS 12	JUL 28	EPFULL adds first-page images and applicant-cited references
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NEWS 18	SEP 09	50 Millionth Unique Chemical Substance Recorded in CAS REGISTRY
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FILE LAST UPDATED: 10 Sep 2009  (20090910/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED:  Jun 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE:  Jun 2009

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=> s methylenetetrahydrofolic acid
           158 METHYLENETETRAHYDROFOLIC
       4898836 ACID
       1711699 ACIDS
       5431857 ACID
                 (ACID OR ACIDS)
L1         123 METHYLENETETRAHYDROFOLIC ACID
                 (METHYLENETETRAHYDROFOLIC(W)ACID)

=> s l1 and ?stabil?
       1397206 ?STABIL?
L2          13 L1 AND ?STABIL?

=> d l2 ibib abs 1-13

L2   ANSWER 1 OF 13  CAPLUS  COPYRIGHT 2009 ACS on STN
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ACCESSION NUMBER: 2006:1206350 CAPLUS
DOCUMENT NUMBER: 145:500132
TITLE: Prevention and therapy of cerebral folate deficiency
PATENT ASSIGNEE(S): Ramaekers, Vincent, Belg.
SOURCE: PCT Int. Appl., 74pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006119589	A2	20061116	WO 2006-BE45	20060504
WO 2006119589	A3	20070726		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: WO 2005-BE74 A 20050511

AB The present invention relates to methods and means to prevent cerebral folate deficiency (CFD) and/or to treat CFD at a very early stage, when CFD has not yet fully developed. It was found that circulating and blocking autoantibodies to folate receptor (FR) represent one of the major causes of CFD and that prognosis improves the younger a child can be treated. The invention as such in particular relates to a method of screening infants and their mothers for the presence of circulating autoantibodies in their serum and/or for low 5-methyltetrahydrofolate (5MTHF) CSF levels, followed by a prompt treatment of a subject in need thereof with a folate supplement in case the testing procedure is pos. Such screening should also be performed for all children or any other subjects as soon as at least 3 of the major criteria of CFD manifest. It was further found that the addition of antioxidants to a folate supplement maintains stability of (5MTHF) and can help restore an impaired 5MTHF uptake in the nervous system due to the circulation of blocking autoantibodies. Avoidance of foods and products, containing proteins with similar amino acid sequences as compared to human FRs, is strongly preferred in the preparation of compds. or food products for the prevention and/or treatment of CFD. The methods and means of the invention have a major impact on the health of the population and can help to reduce the incidence of for instance autism and schizophrenia related to CFD.

L2 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:494414 CAPLUS
DOCUMENT NUMBER: 145:14692
TITLE: Stable tablet formulation of tetrahydrobiopterin
INVENTOR(S): Jungles, Steven; Henderson, Mark; Sluzky, Victoria; Baffi, Robert
PATENT ASSIGNEE(S): Biomarin Pharmaceutical Inc., USA
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006055511	A2	20060526	WO 2005-US41252	20051116
WO 2006055511	A3	20061005		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005306686	A1	20060526	AU 2005-306686	20051116
CA 2581814	A1	20060526	CA 2005-2581814	20051116
EP 1845952	A2	20071024	EP 2005-822282	20051116
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2008520574	T	20080619	JP 2007-541419	20051116
BR 2005017088	A	20080930	BR 2005-17088	20051116
IN 2007DN02764	A	20070803	IN 2007-DN2764	20070413
MX 2007005039	A	20070619	MX 2007-5039	20070426
CN 101132776	A	20080227	CN 2005-80038910	20070514
KR 2007084270	A	20070824	KR 2007-711104	20070516
US 20070270581	A1	20071122	US 2007-563418	20070724
US 20080207626	A1	20080828	US 2008-106621	20080421
US 7566462	B2	20090728		

PRIORITY APPLN. INFO.:	US 2004-629189P	P	20041117
	WO 2005-US41252	W	20051116
	US 2007-563418	A1	20070724

AB The present invention is directed to a stable tablet formulations of tetrahydrobiopterin, processes for producing them, and treatment methods using such formulations. The tablets retain at least about 95% of the active agent after 6 mo storage at room temperature and about 60% humidity. The stable tablet formulations may be used for treatment of conditions associated with elevated phenylalanine levels or reduced tyrosine or tryptophan levels, which may be caused, for example, by reduced phenylalanine hydroxylase, tyrosine hydroxylase or tryptophan hydroxylase activity. For examples, a stabilized tablet formulation was prepared containing (6R)-L-erythro-5,6,7,8-tetrahydrobiopterin (Sapropterin) dihydrochloride polymorph B 33.33, mannitol 57.56, dibasic calcium phosphate 2.18, crosslinked polyvinylpyrrolidone (Kollidon CL) 4.50, ascorbic acid 1.67, riboflavin 0.01, and sodium stearyl fumarate 0.75%, resp. This formulation, containing crosslinked polyvinylpyrrolidone disintegrant, was more stable than a corresponding formulation containing hydroxypropyl cellulose as disintegrant.

OS.CITING REF COUNT:	2	THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT:	2	THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER:	1998:798572 CAPLUS
DOCUMENT NUMBER:	130:136077
TITLE:	Determination of folate patterns in mouse plasma, erythrocytes, and embryos by HPLC coupled with a

microbiological assay
AUTHOR(S): Belz, Susanne; Nau, Heinz
CORPORATE SOURCE: Department of Food Toxicology, University of Veterinary Medicine Hannover, Hannover, D-30173, Germany
SOURCE: Analytical Biochemistry (1998), 265(1), 157-166
CODEN: ANBCA2; ISSN: 0003-2697
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Folates are important cofactors in one-carbon metabolism Disturbances in folate homeostasis and metabolism may be related to an increased risk of cardiovascular disease and carcinogenesis and may lead to congenital malformations, namely neural tube defects. Determination of these compds. in biol. samples is often a problem due to the existence of numerous folate metabolites, their relative instability, and the low contents in serum and most tissues. As existing methods have distinct limitations, we developed a method, which facilitates the separation as well as the sensitive detection of eight folates by coupling HPLC with a microbiol. assay. After a simple sample preparation, including deproteinization and enzymic hydrolysis of folate polyglutamates, exts. were chromatographed, fractions were collected on microtiter plates, and folates were quantitated using the Lactobacillus casei assay. The raw data were processed using a computing system after reconstructing the HPLC chromatogram with the bacterial growth data. Using the described method, the eight physiol. occurring folate monoglutamates could be simultaneously determined The detection limits were 2-20 fmol per injection. The application of the method was demonstrated with the anal. of the folate pattern in milligram or sub-milligram quantities of plasma, erythrocyte, and embryos of pregnant mice during organogenesis. (c) 1998 Academic Press.
OS.CITING REF COUNT: 19 THERE ARE 19 CAPLUS RECORDS THAT CITE THIS RECORD (19 CITINGS)
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1998:687500 CAPLUS
DOCUMENT NUMBER: 130:90019
TITLE: Chemical stability and human plasma pharmacokinetics of reduced folates
AUTHOR(S): Odin, Elisabeth; Carlsson, Goran; Frosing, Roland; Gustavsson, Bengt; Spears, C. Paul; Larsson, Per-Anders
CORPORATE SOURCE: Department of Surgery, Goteborg University, Goteborg, S-416 85, Swed.
SOURCE: Cancer Investigation (1998), 16(7), 447-455
CODEN: CINVD7; ISSN: 0735-7907
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The in vitro stability and plasma pharmacokinetics of 5, 10-methylenetetrahydrofolic acid (CH2FH4), tetrahydrofolic acid (FH4), 5-methyltetrahydrofolic acid (CH3FH4), and 5-formyltetrahydrofolic acid (5-CHOFH4) were studied in view of their potential usefulness in cancer chemotherapy. Anal. of reduced folates was done on a high-performance liquid chromatog. (HPLC) system. The high sensitivity of FH4 and CH2FH4 to oxidation can be circumvented by use of high concns. of the folates, addition of ascorbate, and by thorough exclusion of atmospheric O2. I.v. injection of 200 mg FH4 or CH2FH4 resulted in average peak
concns. of 69.2 ± 3.2 nmol/mL and 46.3 ± 2.6 nmol/mL, resp. The plasma concentration curves support the concept that these highly

oxygen-sensitive reduced folates can be reliably administered as pharmaceuticals to cancer patients through the use of a suitable air-occlusive system for their preparation and administration.

OS.CITING REF COUNT: 13 THERE ARE 13 CAPLUS RECORDS THAT CITE THIS RECORD (13 CITINGS)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1994:436198 CAPLUS
DOCUMENT NUMBER: 121:36198
ORIGINAL REFERENCE NO.: 121:6711a,6714a
TITLE: Method for storage-stabilization of 5,6,7,8-tetrahydrofolic acid and derivative thereof
INVENTOR(S): Torisu, Masaaki; Nagayoshi, Eri
PATENT ASSIGNEE(S): Mitsui Toatsu Chemicals, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 3 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 06065243	A	19940308	JP 1993-183644	19930726
JP 07107064	B	19951115		
PRIORITY APPLN. INFO.:			JP 1993-183644	19930726

AB Powders of 5,6,7,8-tetrahydrofolic acid (I) and derivative thereof are stored under inert gas with exclusion of the outside air and in the presence of a deoxygenating agent at low temperature Folic acid and derivative thereof are effectively stored for a long time without degradation Thus, I containing 1% L-ascorbic acid and a deoxygenation pack (Ageless) having O-absorbing capacity of 50 mL were placed in a brown glass sample tube and after replacing the air inside the container with N, the container was sealed and stored at -20° for 40 days; the purity of I changed from 88.8% to 88.0% vs. 70.6% for the sample without the deoxygenating agent.

L2 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1992:120885 CAPLUS
DOCUMENT NUMBER: 116:120885
ORIGINAL REFERENCE NO.: 116:20197a,20200a
TITLE: Tetrahydrofolate derivatives as modulators for a chemotherapeutic agent
INVENTOR(S): Spears, Colin P.; Gustavsson, Bengt G.; Carlsson, Goran
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9117660	A1	19911128	WO 1991-US3186	19910513
W: AU, BB, BG, CA, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, PL, RO, SD, SU				
RW: AT, BE, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
CA 2082811	A1	19911112	CA 1991-2082811	19910513

CA 2082811	C	20041116			
AU 9179532	A	19911210	AU 1991-79532		19910513
US 5376658	A	19941227	US 1993-174571		19931223
US 5534519	A	19960709	US 1994-326414		19941020
PRIORITY APPLN. INFO.:			US 1990-521712	A	19900511
			WO 1991-US3186	A	19910513
			US 1991-789729	B1	19911112
			US 1993-174571	A3	19931223

AB Administration of 5,10-methylenetetrahydrofolic acid (I) or tetrahydrofolic acid to patients strongly potentiates the antitumor activities and thymidylate synthase-inhibitory effects of 5-FU. I can be used with other drugs which are metabolized to fluorodeoxyuridylate (5-FU metabolite) including floxuridine, ftorafur, and 5'-deoxyfluorouridine. The effect of I was demonstrated with mice bearing s.c. murine colon carcinoma by concomitant injections with 5-FU.

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

L2 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER:	1990:567972 CAPLUS
DOCUMENT NUMBER:	113:167972
ORIGINAL REFERENCE NO.:	113:28414h,28415a
TITLE:	Properties of bacteriophage T4 thymidylate synthase following mutagenic changes in the active site and folate binding region
AUTHOR(S):	LaPat-Polasko, Laura; Maley, Gladys F.; Maley, Frank
CORPORATE SOURCE:	Wadsworth Cent. Lab. Res., New York State Dep. Health, Albany, NY, 12201-0509, USA
SOURCE:	Biochemistry (1990), 29(41), 9561-72 CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Amino acid replacements were introduced in specific sites of phage T4 thymidylate synthase (T4-TS) to assess the role that the changes have on enzyme activity. Each of the conserved amino acids in the active-site region of T4-TS was modified, and the effects that these changes had on the kinetic and phys. properties of this enzyme were measured. The mutations introduced were Pro-155-Ala (P155A), Cys-156-Ser (C156S), and His-157-Val (H157V) with the resulting synthases possessing kcat values of 10.3, 0.008, and 2.70 s-1, resp., relative to that of the wild-type enzyme of 11.8 s-1. Equilibrium dialysis was performed on the wild-type and mutant enzymes to determine the binding consts. for 2'-deoxyuridylate and 5-fluoro-2'-deoxyuridylate, and while in most cases the extent of binding of these nucleotides to the mutant proteins was reduced when compared with wild-type TS, the number of binding sites involved remained .apprx.1 or less for the binary complex and almost 2 for the ternary complex. Heat and urea stability studies revealed that the mutant with the highest enzyme activity, P155A, was the most unstable, whereas spectrofluorometric analyses revealed that the structures of P155A and H157V were perturbed relative to the C156S and wild-type TSs. These studies were in agreement with others implicating the phylogenetically conserved active-site cysteine as playing an essential mechanistic role in the catalytic process promoted by TS. The proximal amino acids on either side of this cysteine, although also highly conserved did not appear to affect the catalytic mechanism directly, but may do so indirectly through their influence on the conformation at the active site as well as on other regions of the enzyme. Amino acid replacements were introduced also into the folate and deoxynucleotide 5'-phosphate binding sites of the T4-phage TS to ascertain the potential role that these amino acids play in the catalytic process. These positions were selected on the basis of previous chemical modification and x-ray crystallog. studies on Lactobacillus casei TS. Amino acid residues 48 and 49, which are in the putative folate-binding site, were

converted from lysines to arginines; in the former case, the mutated enzyme had 7% of the wild-type activity, whereas in the latter, the mutated enzyme still retained .apprx.60% of its activity. Spectrofluorometric studies revealed the K49R T4-TS mutation to affect a conformational change in the enzyme's structure, but little or no change was observed in the spectra of the T4-TS from K48R. The latter enzyme was impaired in its interaction with 5,10-methylenetetrahydrofolate, as evidenced by a >3-fold increase in its Km. On the basis of these and previous folylpolyglutamate fixation studies, it would appear that lysine (Lys)-48 of T4-TS (Lys-50 in L. casei TS) contributes to the binding of folate substrates and their analog to a greater degree than Lys-49 of T4-TS (Lys-51 in L. casei TS). Replacement of arginine (Arg)-137 and Arg-176 in the phosphate binding sites of T4-TS with Lys residues diminished enzyme activity by 70% in the former case, and almost completely in the latter. The TS from R137K did not show a spectrofluorometric shift, whereas TS from R176K did. However, the mutant enzyme from R137G showed a blue shift in its fluorescence spectrum, which was associated with a complete loss in activity. From these studies, it would appear that whereas both Arg-137 and Arg-176 promote nucleotide binding, the latter contributes more to this phenomenon than the former.

OS.CITING REF COUNT: 9 THERE ARE 9 CAPLUS RECORDS THAT CITE THIS RECORD (9 CITINGS)

L2 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1989:612615 CAPLUS
DOCUMENT NUMBER: 111:212615
ORIGINAL REFERENCE NO.: 111:35231a,35234a
TITLE: Role of vitamin B6 in tumor growth
AUTHOR(S): Chuvykin, M. B.
CORPORATE SOURCE: Minsk. Gos. Med. Inst., Minsk, 220798, USSR
SOURCE: Eksperimental'naya Onkologiya (1989), 11(5), 9-13
CODEN: EKSODD; ISSN: 0204-3564
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Russian

AB A review with 49 refs. Vitamin B6 accumulated in the body may stimulate tumor growth as it participates in the formation of polyamines and 5,10-methylenetetrahydrofolic acid and in thymidylate synthetase conformation stabilization. Activation of tumor growth in vitamin B6 deficiency is induced by accumulation of blastomogenic metabolites of tryptophan.

L2 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1988:435926 CAPLUS
DOCUMENT NUMBER: 109:35926
ORIGINAL REFERENCE NO.: 109:6057a,6060a
TITLE: Characterization of the pools of 5,10-methylenetetrahydrofolates and tetrahydrofolates in xenografts of human colon adenocarcinoma
AUTHOR(S): Houghton, Janet A.; Williams, Larry G.; Radparvar, Saeed; Houghton, Peter J.
CORPORATE SOURCE: Dep. Biochem., St. Jude Child. Res. Hosp., Memphis, TN, 38101, USA
SOURCE: Cancer Research (1988), 48(11), 3062-9
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English

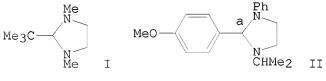
AB Method for measuring polyglutamate forms of 5,10-methylenetetrahydrofolate (CH2-H4PteGlu) and tetrahydrofolate (H4PteGlu), by entrapment in ternary complexes with [6-3H]5-fluoro-2'-deoxyuridylate and Lactobacillus casei thymidylate synthase was developed. The relationship between concentration of CH2-H4PteGlu and complex isolated on nondenaturing polyacrylamide gels was dependent upon the number of glutamyl residues. The relationship was linear

over a 100-fold change in concentration, and the formation of isolable complex was time dependent. Noncovalent complexes formed with PteGlu2-5 could be isolated only at concns. considerably higher than those required for CH2-H4PteGlu1-6, and endogenous deoxyuridylate did not interfere significantly with the assay. The distribution of polyglutamates of CH2-H4PteGlu and the combined pools of CH2-H4PteGlu plus H4PteGlu were subsequently examined in 3 human colon adenocarcinoma xenografts. In each tumor, the pentaglutamate of CH2-H4PteGlu and H4PteGlu was the most prominent species, followed by the hexaglutamate, constituting 68-92% of the CH2-H4PteGlu pool, and >93% of the combined pools. Small percentages of di-, tri-, and tetraglutamates were also detected. Using a catalytic assay, the combined pool of CH2-H4PteGlu and H4PteGlu was estimated 0.5-2.7 μM in cell water, and for CH2-H4PteGlu 0.185-1.7 μM. Using thymidylate synthase purified from colon adenocarcinoma HxVRC5, CH2-H4PteGlu5 stabilized the covalent ternary complex at >200-fold lower concentration in comparison to CH2-H4PteGlu1. Data indicated that in each colon tumor, the concns. of CH2-H4PteGlun or CH2-H4PteGlun plus H4PteGlun were suboptimal for the interaction of 5-fluoro-2'-deoxyuridylate with thymidylate synthase, and would predict for relatively transient inhibition of thymidylate synthase after treatment with 5-fluorouracil. These data support therapeutic modulation to increase the concentration of CH2-H4PteGlun in the treatment of colon adenocarcinomas with 5-fluorouracil.

OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)

L2 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 1979:86276 CAPLUS
DOCUMENT NUMBER: 90:86276
ORIGINAL REFERENCE NO.: 90:13657a,13660a
TITLE: General acid catalyzed imidazolidine hydrolysis. Hydrolysis of 2-(tert-butyl)-N,N'-dimethyl-1,3-imidazolidine and 2-(p-methoxyphenyl)-N-isopropyl-N'-phenyl-1,3-imidazolidine
AUTHOR(S): Fife, Thomas H.; Hutchins, J. E. C.; Pellino, August M.
CORPORATE SOURCE: Dep. Biochem., Univ. Southern California, Los Angeles, CA, USA
SOURCE: Journal of the American Chemical Society (1978), 100(20), 6455-62
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB The hydrolysis rates of aqueous I or II at 30° exhibit similarly shaped pH log rate constant profiles for aldehyde formation; there is a pH-independent reaction at pH >12. As pH is progressively lowered there are successively encountered a H3O+ catalyzed reaction, another nearly pH independent reaction commencing at the high pKa of the imidazolidine ring, and at low pH 2-5 a 2nd H3O+ catalyzed reaction which reflects protonation of the acyclic N atom subsequent to ring opening. In the hydrolysis of I

at pH < 6, 2 well-separated steps are observed in the reaction by using stopped-flow rate data. The reactions correspond to aldehyde formation and subsequent hydration of the aldehyde product. The pH-rate constant profile for the initial step is bell shaped with a maximum at about pH 2. At low pH a monoprotonated species exists as a discrete intermediate prior to the observed reaction. Kinetic general acid catalysis occurs in the initial reaction. This most likely results from the kinetically equivalent general base catalyzed hydrolysis of an intermediate protonated Schiff base, a possibility which is supported by a Broensted coefficient, α, of 0.76. Two steps are observed at 330 nm in the hydrolysis of II at pH <3.5. These steps are ring opening to give a cationic Schiff base and hydrolysis of the Schiff base to p-MeOC6H4CHO. Spectral considerations indicate that the Schiff-base intermediate observed in ring opening is the N-alkyl Schiff base arising from expulsion of the least basic N atom and formation of the most stable iminium ion. The ring-opening reaction is pH independent at pH 0-3.5 indicating reaction of the monoprotonated imidazolidine; the reaction is much slower in D2O than H2O. Proton transfer is taking place in the critical transition state. The reaction must involve proton transfer to the least basic N atom with cleavage of the bond in II. Stabilization of the incipient transition state carbonium ion is the most significant factor in determining the direction of ring opening of unsym. imidazolidines. The reactions of N5,N10-methylenetetrahydrofolic acid are discussed.

OS.CITING REF COUNT: 8 THERE ARE 8 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)

L2 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1978:101109 CAPLUS
DOCUMENT NUMBER: 88:101109
ORIGINAL REFERENCE NO.: 88:15813a,15816a
TITLE: The oxidative cleavage of folates. A critical study
AUTHOR(S): Maruyama, Tadashi; Shiota, Tetso; Krumdieck, Carlos L.
CORPORATE SOURCE: Dep. Nutr., Univ. Alabama, Birmingham, AL, USA
SOURCE: Analytical Biochemistry (1978), 84(1), 277-95
CODEN: ANBCA2; ISSN: 0003-2697
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Alkaline MnO4- oxidation was used to determine the chain length of naturally occurring pteroylpolyglutamates on the assumption that all forms of folates cleave at the C9-N10 bond to produce the corresponding p-aminobenzoylpolyglutamates. The chain length of the latter could be determined by a cochromatog. with synthetic markers. The products of alkaline [(NH4)HCO3 buffer, pH 9.0] MnO4- oxidation of a number of reduced and oxidized, 1-C-substituted and unsubstituted folic acid derivs. were identified, and their yields and stability to the oxidative treatment were determined Unsubstituted, oxidized, and reduced folic acid and N5-formyltetrahydrofolic acid were cleaved at the C9-N10 bond to produce p-aminobenzoylglutamic acid. N5,N10-methenyltetrahydrofolic acid, N5,N10-methylenetetrahydrofolic acid, and N10-formyltetrahydrofolic acid were not cleaved but were oxidized to N10-formylfolic acid which was completely stable to the oxidative treatment employed. N5-methyltetrahydrofolic acid was not cleaved either but was oxidized to N5-methyl-dihydrofolic acid which upon continued oxidation decomposed slowly to unidentified products. The γ-glutamyl peptide linkage was completely stable to oxidation By using p-aminobenzoylglutamic-3,5-3H2 acid, it was also shown that this product, previously thought to be stable to the oxidative treatment, was decomposed by it. The significance of these findings in terms of the errors that may have been introduced in prior estns. of the chain length and pool sizes of the naturally occurring pteroylpolyglutamates is discussed. The possibility of developing a method for the chain length determination of

noncleavable pools of 1-C-substituted folates by using folic-2-14C acid to label the folates in vivo is presented.
OS.CITING REF COUNT: 15 THERE ARE 15 CAPLUS RECORDS THAT CITE THIS RECORD (15 CITINGS)

L2 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1964:10895 CAPLUS
DOCUMENT NUMBER: 60:10895
ORIGINAL REFERENCE NO.: 60:1990c-e
TITLE: 5,10-Methylenetetrahydrofolic dehydrogenase from bakers' yeast. II. Use in assay of tetrahydrofolic acid
AUTHOR(S): Ramasastri, B. V.; Blakley, R. L.
CORPORATE SOURCE: Australian Natl. Univ., Canberra
SOURCE: Journal of Biological Chemistry (1964), 239(1), 106-11
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. CA 57, 6306i. In order that the reaction catalyzed by 5,10-methylenetetrahydrofolic dehydrogenase from bakers' yeast may be used for the assay of tetrahydrofolic acid and 5,10-methylenetetrahydrofolic acid, suitable exptl. conditions have been investigated and a value of 7100 has been obtained for the molar extinction change at 340 mμ for the reaction. An alternative estimation of tetrahydrofolate by the use of this enzyme involves spectrophotometric determination of 5,10-methenyltetrahydrofolic acid in the acidified reaction products. A value of 25,100 has been obtained for the molar absorbancy at 350 mμ of methenyltetrahydrofolic acid in 0.1N HCl for use in this assay. The relative merits of the 2 methods, which give very similar results, are discussed. The stability of tetrahydrofolate and methylenetetrahydrofolate at 0 to 5° in the presence of various buffers at different pH values has been studied. Tetrahydrofolate exhibited greatest stability in tris(hydroxy-methyl)aminomethane-HCl or veronal buffers, pH 7.4, containing 10mM mercaptoethanol. Methylenetetrahydrofolate also showed good stability at this pH with 34m M ascorbate as protecting agent, and was considerably more stable than tetrahydrofolate. No detectable amts. of tetrahydrofolate or methylenetetrahydrofolate were found in protein-free exts. of those tissues of rat that were tested.

L2 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1961:105887 CAPLUS
DOCUMENT NUMBER: 55:105887
ORIGINAL REFERENCE NO.: 55:19938d-f
TITLE: Structure of "active formaldehyde" (N5,N10-methylenetetrahydrofolic acid)
AUTHOR(S): Osborn, M. J.; Talbert, O. T.; Huennekens, F. M.
CORPORATE SOURCE: Univ. of Washington, Seattle
SOURCE: Journal of the American Chemical Society (1960), 82, 4921-7
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB "Active formaldehyde" (I) was synthesized from DL-tetrahydrofolate by suspending it in 0.025M HCHO and adjusting the solution with 5N NaOH to pH 5. The solution was absorbed onto a Solka-floc column and I was eluted with a mixture of 40% EtOH-60% dicarbonate buffer (pH 9.3) containing 10-2 MHSCH22CH2OH. The authenticity of the synthetic material was confirmed by its quant. oxidation to "active formate" via the TPN-linked hydroxymethyltetrahydrofolic dehydrogenase. The following chemical evidence supports the assignment of the structure, N5,N10-methylenetetrahydrofolate to I: the stability to oxidizing agents, the dissociation at

different pH values in the presence of and absence of hydroxylamine, the pH dependence of the rate of formation from HCHO and tetrahydrofolate, and the chemical synthesis via reduction of N5N10-methylenetetrahydrofolate with NaBH4.

OS.CITING REF COUNT: 18 THERE ARE 18 CAPLUS RECORDS THAT CITE THIS RECORD (18 CITINGS)

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